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REMARKS

In the Office Action dated January 13, 2010 (“Office Action”), claims 2-4, 8-20, 38, and 48-50 were considered. The Office Action rejected these claims under 35 U.S.C. § 112, second paragraph, and under 35 U.S.C. § 103.

In the present Amendment, claims 4 and 11 have been amended and claims 19 and 20 have been canceled. Claims 2-4, 8-18, 38, and 48-50 are pending. Applicant respectfully submits that no new matter is introduced by the present amendments.

Claim Objection

The Office Action objected to Claims 19 and 20 stating the claims are drawn to a series of vectors that are not reasonably embraced by the base claims. Applicants have canceled claims 19 and 20.

Claim Rejection Under 35 U.S.C. § 112, second paragraph

The Office Action rejected claims 19 and 20 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the invention (Office Action, p. 3). Applicants have canceled claims 19 and 20.

Claim Rejections Under 35 U.S.C. § 103

The Office Action includes two claim rejections under 35 U.S.C. § 103.

Claims 4 and 8-18 have been rejected under 35 U.S.C. § 103(a) over Godowski et al. (U.S. Patent 5,316,921) in view of Livache et al. (U.S. Patent 5,795,715), Gregory et al. (U.S. Patent 5,932,210), Barber et al. (U.S. Patent 5,716,832), and Good et al. (1997) *Gene Therapy* 4:45-54 (Office Action, pp. 5-10). More specifically, the Office Action indicates that claim 4 uses “comprises” language and imposes no length restrictions. Further, the Office Action

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indicates that Godowski et al. disclose a 56-nucleotide DNA probe that comprises the antisense complement of SEQ ID NO:15 and that one of skill in the art would have been led to make and use a dsRNA comprising SEQ ID NO:15 in view of the prior art (Office Action, p. 7).

Applicants have amended claim 4 to state that “the RNAi is between about 19 and about 29 base pairs in length”. Applicants’ specification supports an RNAi of this length (see, Applicants’ published PCT application WO 2005/095622, at page 19, lines 13-15). As such, Applicants respectfully contend that the 56-nucleotide DNA probe disclosed by Godowski et al. does not read on the RNAi of amended claim 4 and, therefore, amended claim 4 is not obvious over Godowski et al. in view of the cited references. Further, because claims 2, 3, 8-18, 38, and 48-50 depend from claim 4, Applicants also respectfully contend that they have overcome this section 103 rejection as to claims 2, 3, 8-18, 38, and 48-50. Accordingly, Applicants request that this rejection be withdrawn.

Claims 2-4, 8-20, 38, and 48-50 have been rejected under 35 U.S.C. § 103(a) over (i) Abounader et al. (2002) FASEB J. 16(1):108-110, (ii) Mroczkowski et al. (EP 1 243 596 A2), (iii) Elbashir et al. (2002) Methods 26:199-213, and (iv) Tuschl et al. (U.S. Patent Publication No. 2004/0259247 A1); the combination in view of Shi et al. (U.S. Publication No. 2003/0180756 A1). (Office Action, pp. 10-18). Specifically, the Office Action indicates that the siRNA comprising SEQ ID NO:15 would have been one of a number of a finite set of siRNAs that would have been identified during the ordinary course of making an siRNA for c-met (as described in Tuschl et al. and Elbashir et al.) (Office Action, p. 10). Also, the Office Action indicates, while the genus of all possible siRNAs selected according to these criteria many well have been large, the genus was limited by the c-met coding sequence and, “*a priori* each siRNA

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would have been considered equivalent, one to the other, inasmuch as each could be used for the same purpose, leading one of skill to make and use any one of these siRNAs with the expectation each would be capable of performing the function intended (Office Action, p. 16).

The Office Action, however, also notes that the *prima facie* case of obviousness based on structural similarity is rebuttable by proof that the claimed siRNAs possess unexpectedly advantageous or superior properties (Office Action, p. 17). Here, Applicants respectfully contend that the siRNAs of amended claim 4 possess unexpected superior properties as compared to other siRNAs that suppress expression of c-met in human cells. As shown in Figure 1 of the present application, the siRNA comprising SEQ ID NO:15 (included in the vector si-hMet-Ad5²²¹) dramatically suppresses expression of c-met in human cancer cell lines DBTRG, PC-3, and MKN45. As more specifically shown in Fig. 1C, the siRNA comprising SEQ ID NO:15 has superior properties as compared to the siRNAs comprising SEQ ID NOs: 13 and 14 (included in vectors si-hMet-Ad5¹⁶ and si-hMet-Ad5⁶², respectively). Applicants investigated the ability of each of si-hMet-Ad5²²¹, si-hMet-Ad5¹⁶, and si-hMet-Ad5⁶² to suppress c-met expression; and, the inhibitory effect was strongest with si-hMet-Ad5²²¹ (Applicants' published PCT application WO 2005/095622, at page 25, lines 3-7). It is not expected that si-hMet-Ad5²²¹ would exhibit greater suppression of c-met than either si-hMet-Ad5¹⁶ or si-hMet-Ad5⁶². As such, si-hMet-Ad5²²¹ (siRNA comprising SEQ ID NO:15) shows unexpected superior properties as compared to si-hMet-Ad5¹⁶ or si-hMet-Ad5⁶² (siRNAs comprising SEQ ID NOs:13 and 14). [Note: a marked reduction in c-met expression also was shown when the effect of si-hMet-Ad5²²¹ was investigated in four human ovarian cancer cell lines (see, Figs. 11A-11D)]. Accordingly, because the siRNAs of amended claim 4 possess unexpectedly advantageous or superior

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properties, Applicants respectfully contend that this section 103 rejection should be withdrawn. Further, because claims 2, 3, 8-20, 38, and 48-50 depend from claim 4, Applicants respectfully contend that they have overcome this section 103 rejection as to claims 2, 3, 8-20, 38, and 48-50 and, therefore, this rejection should be withdrawn with respect to these dependent claims.

Rejoinder of Claims 48-50

Claims 48-50 depend from linking claim 38. Accordingly, given that claim 38 now is in condition for allowance, Applicant respectfully requests that claims 48-50 also be allowed.

CONCLUSION

Applicants respectfully request entry of this Amendment and Response, withdrawal of all bases for rejection, and allowance of claims 2-4, 8-18, 38, and 48-50 in due course. The Examiner is invited to telephone Applicants' undersigned representative at (616) 949-9610 to discuss any outstanding issues.

Respectfully submitted,

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